

- A 1
- (b) the epitope protection positions for the second epitope region are selected from the group consisting of 25, 26, 27, 46, 47, 48, 49, 50, 51, 52, 53, 54, 91, 99, 100, 101, 102, 127, 128, 129, 130, 131, 132, 133, 134, 136, 137, 138, 140, 141, 144, and 145 of the amino acid sequence of subtilisin BPN' set forth in SEQ ID NO:1; and
- (c) the epitope protection positions for the third epitope region are selected from the group consisting of 9, 10, 22, 23, 24, 62, 63, 143, 146, 154, 155, 156, 157, 172, 173, 187, 189, 195, 197, 203, 204, 253, 254, 256, 265, 267, 269, 271, 272, and 275 of the amino acid sequence of subtilisin BPN' set forth in SEQ ID NO:1.
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5. A protease conjugate according to Claim 4 wherein the parent amino acid sequence is selected from the group consisting of subtilisin BPN', subtilisin Carlsberg, subtilisin DY, subtilisin 309, proteinase K, thermitase, Protease A, Protease B, Protease C, and Protease D.

6. A protease conjugate according to Claim 5 wherein:

- A 2
- (a) the epitope protection positions for the first epitope region are selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 12, 17, 40, 41, 43, 67, 86, 87, 89, 206, 209, 214, and 215;
- (b) the epitope protection positions for the second epitope region are selected from the group consisting of 27, 47, 48, 50, 52, 102, 127, 128, 130, 131, 132, 134, 138, and 141; and
- (c) the epitope protection positions for the third epitope region are selected from the group consisting of 22, 23, 24, 143, 146, 155, 173, 189, 197, 203, 204, 253, 254, 265, and 275.

7. A protease conjugate according to Claim 6 wherein the epitope protection positions for the first epitope region are selected from the group consisting of 1, 2, 3, 4, 5, 17, 40, 41, 43, 67, 86, 87, 89, and 214.
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11. A protease conjugate according to Claim 10 wherein the first polypeptide is selected from the group consisting of subtilisin BPN', subtilisin Carlsberg, subtilisin DY, subtilisin 309, proteinase K, thermitase, Protease A, Protease B, Protease C, and Protease D.
12. A protease conjugate according to Claim 11 wherein the first polypeptide is covalently attached to the linking moiety or the protease moiety at a position of the first polypeptide selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 9, 10, 12, 17, 22, 23, 24, 25, 26, 27, 36, 40, 41, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 62, 63, 67, 86, 87, 89, 91, 99, 100, 101, 102, 127, 128, 129, 130, 131, 132, 133, 134, 136, 137, 138, 140, 141, 143, 144, 145, 146, 154, 155, 156, 157, 172, 173, 187, 189, 195, 197, 203, 204, 206, 209, 210, 212, 213, 214, 215, 216 253, 254, 256, 265, 267, 269, 271, 272, and 275.

19. A protease conjugate according to Claim 1 additionally comprising one or more supplementary moieties selected from the group consisting of small molecules, polypeptides, and polymers.

Remarks

Claims 1-21 are pending in the present application. No additional claims fee is due.

Claims 1, 5, 6, 7, 11, 12, and 19 have been amended. Support for the amendment to Claim 1 can be found on page 5, lines 13-15 of the specification. Support for the amendment to Claim 19 can be found on page 13, lines 24-29 of the specification. Claims 5, 6, 7, 11, and 12 were amended as a matter of form. Claim 7 was amended to include elected position 89. Attached hereto is a marked-up version of the changes made to the claims by the current amendments. The attached page is captioned "Version with markings to show changes made."

Response to the Office Action

Information Disclosure Statement

The Office Action indicated that three publications numbered 43, 52, and 53 lack publication dates, a necessary element for consideration. In response, Applicants are submitting the following publication dates: Publication 43: 1981; Publication 52: 1990; Publication 53: 1993 (please see enclosed publications). Applicants contend that the submission of the publication dates provide the necessary element for consideration.